The remaining eight children improved. This was demonstrated by the comments of the parents. Increase in exercise tolerance was pronounced, and one child climbed Snowdon within a year of operation, a feat which she could not previously have attempted. Her greater capacity for exertion was due in part to easier breathing, but more to a greater power in her legs. As her mother put it, "Her legs are twice the size." Four children noticed that their feet were no longer cold, and three of them were relieved of cramps.

The most readily measurable criterion is the effect on blood pressure. Before operation the 11 children showed only slight fluctuations in blood pressure, and 11 controls (identical except that they had not been treated surgically) have shown a slight increase of pressure during the period of observation. The effect of resection is shown in Fig. 4, where immediate pre-operative pressure is compared with the post-operative pressure. The two cases treated by subclavian aortic anastomosis showed improvement in every way comparable to that from an end-to-end aortic junction.

In successful cases the blood pressure not only fell immediately but continued to fall for some weeks after operation. This can be demonstrated by comparing the blood pressure at the time of discharge with that recorded when the patients were last seen (Fig. 5). The finding encourages the hope that improvement may be permanent in most of these children.

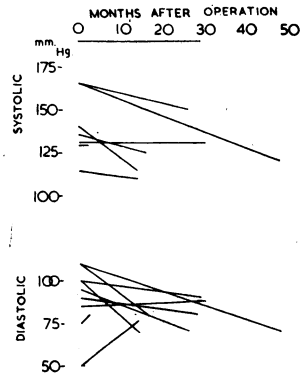


FIG. 5. — Blood-pressure records at time of discharge from hospital and when last seen.

What happens at the site of anastomosis is uncertain, but the continued fall of blood pressure is presumptive evidence that in older children the junction usually grows with the child. We have not seen an aneurysm develop, and we imagine that it is less likely to happen in the relatively healthy tissues of a child's aorta than in the degenerated vessels of an adult. On the other hand, post-operative stricture has occurred in two patients. In one of them, an infant, the stenosis formed quickly and completely after an entirely satisfactory resection and a good anastomosis. It is difficult to avoid the impression that some inherent quality of the infant's aortic tissue played a part in the recurrence. In the older child stenosis was less severe and developed less rapidly.

The cause of the hypertension in coarctation remains a matter of controversy. When circumstances made it necessary to occlude the descending aorta for several days in a child who had well-developed collateral channels, the blood pressure in the arms rose from 145/110 to 240/170. It fell again immediately after a successful operation ten days later. The blood pressure remained high in both patients who developed post-operative stenosis. These observations suggest that a purely mechanical factor plays a considerable part in the hypertension, but the progressive, less spectacular, fall of blood pressure which follows the immediate improvement points to a gradual reduction of vascular tone, and perhaps may be due to a falling concentration of pressor substances in the circulating blood.

Impressions

Coarctation seems to be potentially a dangerous disease, and for any individual patient it is difficult to predict the future. When a baby with coarctation has symptoms of heart failure, and when this failure shows no response to medical treatment, he is unlikely to survive more than a few months unless treated surgically: the only post-operative death in this series occurred in an infant previously in heart failure. During the rest of the first decade a child with coarctation appears to be comparatively safe, but the hazard to life seems to increase greatly after puberty. Operation has seemed to us to be easier and safer in children than in adult subjects, and has usually been followed by a fall of blood pressure which has been progressive over a period of several weeks. Stricture formation may follow operative treatment; it is likely to have more serious consequences in infancy, and on present evidence, therefore, we feel that the best age for operating on cases of coarctation is the second half of the first decade. Earlier operation may be essential when there have been symptoms of heart failure or of subarachnoid haemorrhage.

Summary

Evidence is presented to show the prognosis of coarctation of the aorta. If a baby has coarctation and symptoms of heart failure, and if the failure is slow to respond to medical treatment, death is probable within the course of a few months unless treated surgically.

During a period of five years at the Children's Hospital, Birmingham, 30 infants died from coarctation within six months of birth. During the rest of the first decade a child with coarctation appears to be comparatively safe, but the hazard to life increases again at puberty and the chances of reaching the age of 40 are poor. Operation has proved easier and safer in children than in adult subjects, and has usually been followed by a fall of blood pressure which has been progressive for a period of several weeks. Stricture formation may follow operative treatment: two examples of this are given. We believe that the second half of the first decade is the best time to operate on cases of coarctation.

We thank our colleagues for referring patients to us, Dr. H. S. Baar for post-mortem reports, and Dr. Roy Astley for his constant help.

REFERENCES

Abbott, M. E. (1928). *Amer. Heart J.*, **3**, 574.
Blackford, L. M. (1928). *Arch. intern. Med.*, **41**, 702.
Reifenstein, G. H., Levine, S. A., and Gross, R. E. (1947). *Amer. Heart J.*, **33**, 146.

OUTBREAK OF FOOD-POISONING FROM BREAD MADE OF CHEMICALLY CONTAMINATED FLOUR

BY

G. M. DAVIES, M.B., Ch.B., D.P.H.
Medical Officer of Health, Pontardawe Rural District Council

AND

IEUAN LEWIS, M.B.E., F.S.I.A.
Senior Sanitary Inspector, Pontardawe Rural District Council

The outbreak of food-poisoning here reported upon is characterized by two factors: the widespread nature of the inquiry, and the unusual nature of the contaminant. The extensive inquiry was necessary in that, contamination during transport being suspected, it was essential to establish the full facts in order to prevent recurrence. The unusual nature of the contaminant, endrin, is indicated by the fact that no previous record has been found of endrin-poisoning since the insecticide became generally available in March, 1954. It is of interest, therefore, to report on the means by which the contaminant was identified and to provide clinical details of endrin poisoning.

Description and Location of Area.—The Rural District of Pontardawe is situated in Glamorgan some seven

miles to the north-east of Swansea. It has a population of 32,520 and an acreage of 35,000. The main centre of population is in the Swansea Valley, which runs through the area from south-west to north-east, with the town of Pontardawe at its centre. The principal industries of the area are coal-mining, steel and tinplate manufacture, and nickel refining. The outbreak was entirely confined to the lower portion of the valley, which embraces the six miles between Clydach and Godrergraig.

Inquiry into Outbreak

At 4 p.m. on May 2 the public health department was informed by telephone that 10 men at a local works had been taken violently ill during the course of the day. Immediate inquiry showed that their places of work and illness so differed that gas and fume escape could be eliminated; food-poisoning was therefore suspected. Of the 10 men, seven had been sent home, one had remained at work, while two had been admitted to hospital.

Further inquiries were immediately made at the homes of the persons concerned and details taken of the food eaten at the works that day. It was found that in every case the only common factor was white bread rolls, and in most cases such rolls and a cup of tea had provided the only meal before the illness. This fact was established at 7 p.m. the same evening, and a visit was paid at once to the bakery where these rolls had been manufactured. The baker was asked to provide details of his bakings for that day's consumption, and it was found that the works rolls were manufactured from white patent flour while his bread was manufactured from national flour.

He had during the morning of May 2 returned two sacks of national flour to his suppliers because of an indefinable odour. It should be noted that at this time the only commodities implicated were white bread rolls, and the illnesses were confined to persons working in the local works. At 11.30 p.m., however, a medical practitioner telephoned that a person having no connexion with the works and not having consumed rolls from the works supplies but from the same bakery had collapsed in similar circumstances to the other cases. Inquiries were therefore pursued through the night in order to ascertain whether or not there was sufficient prima facie evidence to warrant a B.B.C. warning being given to the public the following morning, May 3.

By 6 a.m. on May 3 it was considered that a broadcast warning was necessary, and the police were asked to transmit a message through the appropriate channels. This message, which was broadcast on the 8 a.m. and 9 a.m. news, instructed all persons who might have purchased white bread rolls in the Pontardawe area on May 2 to destroy them as it was possible that some might have been chemically contaminated. That the warning was justified was apparent during the course of that day, May 3, when 47 cases were notified among the general public. In every case it was established that bread manufactured at the same bakery on May 2 had been consumed by the patients.

It is estimated that the amount of contaminated bread available for consumption in the area placed approximately 1,500 persons under risk. The word "destroyed" was used advisedly in the broadcast, as it was thought that the public might otherwise dispose of the bread in unsatisfactory circumstances. It is known that in one instance the bread was fed to 12 chickens, all of which died.

Inquiries were complicated by the fact that the 10 persons ill on May 2 at the works had eaten white bread rolls made from white patent flour, while the 47 people taken ill on May 3 had eaten bread manufactured from national flour. A number of samples were obtained of the actual bread, and the Welsh Board of Health, with whom the local health department was in close contact, made arrangements for analysis of the bread samples by the Department of the Government Chemist, London. On Monday, May 7, the wooden floor of the bakery storeroom was closely examined and found to be giving off an aromatic odour at a point where the baker indicated a sack of national flour to have rested. This section of the floor, some six inches (15 cm.) square, was thoroughly scraped with a wire brush and the dust obtained also forwarded to the Government Chemist through the Welsh Board of Health.

The two sacks returned by the baker were traced to a depot at Swansea, and on examination one was found to have some aromatic odour at the bottom of the sack. Samples of this sacking and the flour immediately below were again sent for analysis. The depot foreman of the flour company was able through his invoices to trace that this flour was loaded into a rail wagon at Cardiff on April 21, discharged at the Swansea depot on the 25th, and delivered immediately to the baker.

The number of the rail van was passed to the transporters and they were asked to trace both its present location and its movements and contents prior to April 21. On May 14 a report was received from the Government Chemist that after a long and difficult analysis the contaminant had been identified as endrin, a chemical used in horticultural sprays against various pests. It was also found that this chemical was manufactured only in the U.S.A. and that only one firm imported it into this country. The firm concerned was given the number of the rail wagon and asked to trace whether it had ever been used by them, and, in addition, whether they had received any complaints that endrin products had leaked during transit.

On May 22 the transporters reported that the rail wagon had been found near Cambridge, and it was later learned that it would be brought to London under seal for further examination. On May 28 representatives of the public health department, the flour firm, the chemical importers, and the transporters discussed the question in London, when it was found that leakage of endrin during transit had occurred on February 20, 1956, and that further inquiry had shown the wagon in which the spillage had occurred to be the same as that in which the contaminated flour was later transported.

It was stated that endrin was dissolved in xylene for normal spraying purposes and that the spillage into the wagon had occurred at a concentration some 800 to 1,600 times higher than that at which it was sprayed in the field. It was appreciated that under normal conditions xylene evaporates fairly quickly and that some two months had elapsed between spillage and suspected contamination of the flour, but it is felt, however, that the problem of non-evaporation is of less significance than the fact that endrin was spilled in a wagon which subsequently carried flour found on analysis to contain endrin. It was arranged at this meeting that the wagon floor be sectioned and scraped and the scrapings analysed for the presence of endrin. The laboratory reports of endrin content of the various samples are shown in the Table.

Symptoms

As a result of the episode described previously 59 persons were notified by local general practitioners as suffering from food-poisoning, and it is probable that at least a hundred more felt unwell but did not call in their doctor. All the illnesses followed the eating of bread rolls, "batches," or loaves made from flour now known to have been contaminated with endrin.

The main symptoms were in every case suggestive of a disturbance of the central nervous system. The severity of the attack appears to have been related directly to the amount of bread eaten: about three or four slices or two or three rolls were usually sufficient to produce a convulsion. The time of onset was somewhat variable. In most cases symptoms occurred about three hours after ingestion. Where the interval was only half to one hour it was usually found that some of the bread had also been eaten at an earlier meal as well.

Approximately 30 of those affected suffered from a convulsion of sudden onset. With no warning, they fell to the ground unconscious wherever they happened to be, and

Tabulated Results, with Comments, of Samples Analysed by the Department of the Government Chemist, London

Sample	Date	Description	Origin	Endrin Content		Remarks
				%	p.p.m.	
1	5/5/56	White patent flour	Shaken from empty sack "A" at bakery	Nil	Nil	
2	5/5/56	,, ,, ,,	,, ,, ,,	0·02	200	Probably contaminated by storeroom contact with national flour sacks (sample 8 below)
3	5/5/56	,, ,, ,,	Shaken from empty sack "B" at bakery	0·05	500	
4	5/5/56	,, ,, ,,	From sack in current use	Nil	Nil	
5	7/5/56	Floor scrapings	Wooden floor of bakery flour storeroom	0·96	9,600	Scraped from place where used sack of national flour had rested from 25/4/56 to 2/5/56
6	7/5/56	Loaf	Mix "A" May 2	0·015	150	Remaining portion of loaf which had caused illness to one person
7	8/5/56	National flour	Taken from *top* of Sack 1, returned full by baker	Nil	Nil	These samples were taken from two full sacks of national flour returned to flour depot by the baker on May 2, and sampled there
8	8/5/56	,, ,,	Taken from *bottom* of Sack 1, returned full by baker	0·55	5,500	
9	8/5/56	Sacking	Cut from bottom of Sack 1	0·15	1,500	
10	8/5/56	National flour	Taken from Sack 2, returned full by baker	Nil	Nil	
11	8/6/56	Floor scrapings	Scraped from bottom of wagon	11·6	116,000	Traces of endrin in five other flour samples of same wagon. Presence of wheat starch in all samples

several injured themselves in so doing. Eyewitnesses, including local doctors, have recorded that the convulsions were epileptiform in character, with frothing at the mouth, facial congestion, and very violent convulsive movements of the limbs, sometimes accompanied by an arching of the vertebral column. Two persons suffered from a shoulder dislocation during a convulsion. After a period of several minutes the patient became quiet but remained semi-conscious in most instances for a further 15 to 30 minutes. Three of those affected had more than one convulsion, and in one case, that of a young farm hand who had eaten almost a whole loaf, convulsions followed one another in quick succession for about an hour.

Symptoms also followed a definite pattern in the less acute cases. These patients first noticed that they were becoming dizzy, with weakness in the legs, abdominal discomfort, and nausea. Few actually vomited, but those who did, whether spontaneously or after being given a salt-and-water emetic, recovered more rapidly. In many cases the feeling of weakness increased; the patient became disorientated and felt as if he were falling forward. There was considerable confusion of thought and some actually imagined at the time that they were "going mad." At this stage some of them became a little aggressive; one or two said that the top half of their head felt as if it was solid. Several noticed that they became temporarily deaf.

Recovery was comparatively rapid even in cases where there had been a convulsion, and by the following day most of those affected felt fairly well. However, a few complained of weakness, insomnia, and loss of appetite for several days. A small minority remained away from work for two to four weeks complaining of headaches, lethargy, weakness, and anorexia, but the symptoms of some of this latter group may have been psychological in origin.

Often the whole family became ill after eating the bread, but in some cases, although all had eaten the bread, only one person became ill. It is interesting to note that very few children were affected. Among the notified cases there were only three children of 10 years of age or younger, the youngest being a girl of 8½. In all, 17 persons were sent to hospital, the majority of whom had practically recovered by the time they were admitted. Case histories show that in no cases were abnormal neurological signs discovered with the exception of some abnormal findings in the seven patients who were examined electroencephalographically. The electroencephalograms are now being repeated in some of these cases.

Case 1.—A steelworker aged 21 ate some of a contaminated batch for supper on May 2. After he had gone to bed he felt a little dizzy and could not sleep during the night. Next morning he ate more of the batch for breakfast and felt weak and giddy during the morning. At midday he had his lunch, eating four slices of the same batch. He then went to work feeling dizzy and thirsty, and having an unpleasant taste in his mouth, with a certain amount of nausea. At 4 p.m. he suddenly fell down unconscious and remained so for about 15 minutes. He was admitted to Morriston Hospital at 6 p.m., having dislocated his left shoulder during the convulsion. On arrival at hospital he was quite conscious and there were no abnormal, neurological, or other signs. He remained in hospital three days and was discharged apparently quite well. An electroencephalogram taken four and a half hours after the convulsion suggested a paroxysmally unstable element, finding expression chiefly in the right posterior area and temporal or central areas.

Case 2.—A male member of the steelworks maintenance staff aged 28 ate three white rolls at 8 a.m. on May 2. He felt perfectly well during the morning, but while out for a walk on the road outside the works at about 11.15 a.m. he fell in a "fit" and was unconscious for approximately 20 minutes. He was brought home and went to bed feeling giddy and suffering from nausea. He slept well that night and felt no ill effects. At 12.30 p.m. on May 3, however, he ate four slices from a contaminated batch, and three hours later felt ill, weak, and dizzy once more. He returned to bed, and at 6 p.m. had a further convulsion, after which he remembered very little for about two hours. He again slept well and awoke fully recovered on the morning of May 4, except that for some days afterwards he suffered from vertigo on lying down. He returned to work on May 7. Five weeks after his illness he stated that he still felt a little vertigo on lying down.

Case 3.—A male clerk aged 50 ate three slices from a contaminated batch at about 1 p.m. on May 2. At 4 p.m. he found he could not concentrate, and at 5 o'clock he returned home from the office with a slight feeling of nausea. When he reached home he became confused in thought and felt very irritable and was perhaps a little aggressive. He felt unbalanced, and described the symptoms as feeling as if he was "going mad." He suffered from lack of orientation. The top of his head felt like a stone, and he noticed a feeling as of insects crawling on his left arm. His legs became very weak and felt heavy, and on looking in the mirror he noticed that his pupils were widely dilated. These symptoms continued during the early part of the evening, and at 8 p.m. he went to bed. From 10 p.m. until 3 a.m. he was unable to sleep, only dozing fitfully. By 3 a.m. he felt much better and slept well until 6 a.m. He got up and ate a good breakfast. About 10 o'clock, while at the office, he noticed a slight recurrence of mental confusion and disorientation, but this lasted only for about 15 minutes. He was off colour and weak for a further 72 hours. He stated that in spite of his mental confusion he was able by a great effort to collect his thoughts from time to time.

Case 4.—A man aged 24, a clerk at the steelworks, ate two white bread rolls in the works canteen at 10.45 a.m. on

May 2. Two hours later he felt "hot" and not very well, and walked to the top of the stairs to get some fresh air. He apparently had a convulsion and remembers nothing for 30 minutes. He fell downstairs, severely bruising the area around his right eye. He went home and soon felt much better, but was off his food for several days. He remained away from work for eight days.

Case 5.—A pharmaceutical chemist, aged 46, ate five slices, at 1 p.m. on May 2, of a contaminated batch which had been quite recently baked. Two hours later he felt hazy and could not concentrate. He had some flatulent discomfort but did not vomit. He became giddy and was stated to be a little aggressive and to be blinking his eyes frequently. He gradually improved but did not feel quite well. At 7.15 p.m. he ate a further five slices from the contaminated batch, and, although he still did not feel well, he attended a meeting where he was chairman. He found that he could not concentrate again, and at 8 p.m. he suddenly became rigid and fell unconscious. He bruised his nose and cut his scalp in falling and there was considerable bleeding. During the convulsion his arms and legs were jerking. He was unconscious for about 15 minutes and was removed to hospital. He thinks that he vomited before he arrived. It is stated that he was fully conscious on arrival at the hospital and there were no abnormal neurological signs. However, he still felt hazy and very restless that night, sleeping badly. Next day he felt much better. An electroencephalogram was taken approximately 20 hours after the fit. It was reported to be abnormal and suggestive of some irritative condition or mild unstable element finding expression chiefly to the right of midline in central and also to some extent in temporal areas. A further electroencephalogram was taken four days after the convulsion and was reported as showing considerable improvement, but still not typically normal, being reminiscent of persons experiencing a state of tension or anxiety.

Case 6.—A tinplate worker aged 47 ate half a loaf from a contaminated batch for supper on May 2. He felt peculiar during the night and could not sleep. At 9 a.m. he ate a further half loaf for breakfast. He did not feel like going to work, and by midday he was feeling very ill. He felt numb from the waist down, was dizzy, and had considerable confusion of thought. At 2 p.m. he had a convulsion and fell. He was noticed to be black in the face and frothing at the mouth, and his limbs were jerking. The convulsion lasted three or four minutes, and he remembers nothing for about half an hour afterwards. He was sent to hospital, where on admission his condition was satisfactory and a clinical examination was negative. He was in hospital for two days and had no after-effects.

Case 7.—A housewife aged 46 ate two slices of a contaminated batch at about 10 p.m. on May 2. She awoke at 2 a.m. feeling ill, trembling all over, perspiring, and very weak. She vomited and felt much better afterwards. At 9 o'clock the following morning she ate three further slices from the contaminated batch. She did not feel very well during the morning, and by midday she was again trembling with weakness and had abdominal discomfort and nausea. There was considerable confusion of thought. She was disoriented, was deaf, and her eyes were slightly dim. She was admitted to hospital. On the way down in the ambulance she vomited and felt slightly better afterwards. On arrival at the hospital her condition was good and clinical examination was negative. She remained in hospital for two days and had no after-effects.

Case 8.—A schoolgirl aged 16 ate four or five slices from a contaminated batch for supper on May 2. She awoke at 3 a.m. and could not sleep for the rest of the night, feeling weak and having a sensation of nausea. She felt much better next morning but did not go to school. At 9 a.m. she ate a further four slices from the batch. At 11 a.m. she felt ill and was noticed to be extremely pale. She lay down, and at 11.30 she had a convulsion, becoming unconscious. She was black in the face, frothing at the mouth, and remained unconscious for about 20 minutes. She came round and felt weak and drowsy. Half an hour later she had a second convulsion and was again out for 15 to 20 minutes. Whilst in the ambulance she had a third similar convulsion, after which she vomited. On admission to hospital she was pale and drowsy. Nothing else abnormal was recorded. She remained in hospital for two days with apparently no after-effects.

Case 9.—A schoolgirl aged 8½ ate three slices of a contaminated loaf at 5 p.m. on May 2, but felt quite well. For breakfast on May 3 she ate a further two or three slices of the loaf with no ill effect. However, by 5 p.m., she felt "funny in her tummy," had a headache, and looked heavy about the eyes, but ate her tea, at which meal she consumed a further three slices of the bread. She played during the evening but was not quite well. She went to bed at 8 p.m., and about 8.30 p.m. her father called upstairs to tell her to keep one of the other children quiet. He received no reply, and, on going up to investigate, found the child lying on the floor in a dazed condition. She stated that she did not know where she was. He picked her up and placed her on the bed, whereupon she had a convulsion, with considerable jerking of her arms and legs, and fell off the bed again. She was semi-conscious for about half an hour; then she vomited a little and felt much better. She slept well during the night and was quite all right next day.

Case 10.—This patient, a blind man aged 55, attends an occupational centre. At 1 p.m. on May 3 he ate four slices of bread from a contaminated batch. These formed part of his lunch, which he ate as sandwiches whilst away for the day at the blind institute. About 4 p.m. he felt dizzy, "off his balance," and felt as if he was falling forward. He returned home, and at 5.15 ate two more slices of bread from the same contaminated batch. About an hour later he fell in a convulsion, cutting the top of his head. He was removed to hospital and remained there for two days; it was noted on admission that he was shocked but fully conscious. He had a laceration over the right parietal bone but no bony injury. He felt weak for several days after his return from hospital.

Case 11.—A male clerk aged 18 ate three slices from a contaminated batch for his lunch on May 3. He felt quite well, and at 5 p.m. ate a further four or five slices from the same batch. Again he felt no ill effects, but at 6.30 he fell in a sudden convulsion and was removed to hospital. On arrival he was conscious but feeling dazed. His condition was stated to be satisfactory. He felt dizzy for a further two days after his return home and remained away from work for five days.

Case 12.—This patient, a woman aged 22, was a chemist's assistant. At about 8 a.m. on May 3 she ate one round of toast made from a contaminated batch. At 11 a.m., while working in the chemist's shop, she began to feel sick and dizzy, and says that she saw double for a while. She came home at 1 p.m. suffering from nausea and feeling as if she was going to fall. She vomited a little and spent the afternoon in bed. She felt somewhat better, and at 4.30 p.m. had tea, eating three slices from the contaminated batch. She was feeling much better during the evening, but at 8 o'clock suddenly had a convulsion and became unconscious. She remembered nothing for about an hour afterwards. On admission to hospital she was stated to be quite well, with no abnormal signs. An electroencephalogram taken 19 hours after the convulsion was reported to be outside normal variation, suggesting a non-specific unstable element finding expression in the central and posterior areas generally. She remained in hospital for a week. She stated that she slept badly for a further week after return home and that her appetite was still rather poor. She was off work for five weeks.

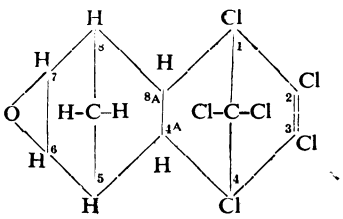
Case 13.—A farmer aged 33 consumed four or five slices from a contaminated batch at about 1 p.m. on May 3. He continued his work and felt quite well during the afternoon. About 5 p.m., whilst he was driving a tractor in a

field which he was harrowing, he fell and remembers nothing until he found himself lying on the ground, the tractor having continued on its course and run into a hedge. He got up and returned home, and for about an hour he felt ill, with some confusion. At 6 p.m. he vomited and went to bed. He slept well and felt much better the following morning, but was a little weak during that day. There were apparently no after-effects.

Case 14.—A farm hand aged 18 ate the greater part of a contaminated loaf at 10 a.m. on May 3. About two hours later he had a fit while driving cattle on the road. He fell unconscious and was noticed to be purple in the face and frothing in the mouth; his arms and legs were jerking. He became partially conscious after three or four minutes, and then had a second fit. During the next hour he had a series of similar fits each lasting a few minutes with a period of semiconsciousness between them. He was removed to hospital, and on admission was said to be drowsy and confused. There were no abnormal neurological signs, and he recovered within a few hours. An electroencephalogram taken 48 hours after the convulsion was reported as being abnormal, but the possibility of underlying behaviour disorder was suggested in this case. This boy is at an approved school and is boarded out with local farmers. On discharge from hospital five days later he did not return to the farm where he was working, but went back to the farm school from which he originally came.

Chemistry of Endrin

The word "endrin" is a coined common name for a pure chemical with the following structural formula :



Endrin is the newest member of a triumvirate of insecticides, the others being "aldrin" and "dieldrin." All are closely related both structurally and in that all three have their origin in dicyclopentadiene, a hydrocarbon found in small quantities in distillates from "cracked" petroleum or coal-tar. Endrin, however, is the most versatile insecticidally because in addition to the range of insects killed by dieldrin it also gives control of many caterpillar and aphide pests.

At present endrin is produced at the Shell plant at Denver, Colorado, U.S.A., but will soon be produced also at the new insecticide plant of the Royal Dutch Shell Group at Pernis, Rotterdam.

Endrin is soluble in aromatic hydrocarbons and ketones, sparingly soluble in alcohols and paraffin hydrocarbons, and insoluble in water. As marketed for formulation purposes, it is a pale buff granular product containing 90–95% of endrin, is easily ground, and has a faint "medicinal" smell. It became available for field evaluation outside the U.S.A. towards the end of 1952 and was generally available in March, 1954.

Formerly known as compound 269, this new insecticide has been found extremely useful in the field, exercising control over cotton and tobacco pests, borers of cane, rice, and coffee, moths, caterpillars, and aphides. In this country its main use to date has been in the fruit-growing industry for control of apple aphis, apple sucker, winter moth caterpillar, tortrix caterpillar, and apple saw-fly.

The manufacturers recommend sensible precautions with regard to endrin, while emphasizing its toxicity to be of a lower order than that exhibited by the older anticholinesterase or phosphate insecticides or by arsenic compounds.

This insecticide is comparatively new, and present information must necessarily be regarded as interim.

Toxicity of Aldrin, Dieldrin, and Endrin

So far as is known no previous cases of endrin poisoning have been reported in human beings, but cases have occurred of poisoning by aldrin and dieldrin (Princi, 1952), which are chlorinated hydrocarbons similar to endrin, and are also used as pesticides.

Endrin is an isomer of dieldrin. In these cases the early symptoms are reported as being headache, nausea, vomiting, general malaise, and dizziness. Where the amount of intoxicant which had been absorbed was small further symptoms rarely developed. However, when larger doses were taken central nervous symptoms occurred. These were characterized by convulsions which were clonic and tonic in character. If the dose was excessively large, the central nervous symptoms occurred without any other premonitory symptoms. The convulsions were sometimes followed by coma. Hyperexcitability and hyperirritability were common. Thus it is seen that the symptoms of poisoning by these substances are very similar to those caused by endrin in the outbreak at present under review.

One case of aldrin poisoning which occurred in 1951 has been described in considerable detail (Spiotta, 1951). It refers to a 23-year-old farmer in the United States of America who intentionally drank from a coca-cola bottle containing an aldrin mixture. He was estimated to have ingested 25.6 mg. of aldrin per kg. of body weight. In spite of gastric lavage generalized convulsions began within 20 minutes and persisted until large amounts of barbiturate had been given. During one of these convulsions he dislocated a shoulder. Later an electroencephalogram revealed generalized cerebral dysrhythmia. The rhythm did not become essentially normal until five months had elapsed. Haematuria and albuminuria appeared on the second day and persisted for 18 days. Although symptoms in this case persisted for 12 days complete recovery ensued and there appeared to have been no permanent kidney or liver damage. In addition no permanent organic brain changes were found either by means of electroencephalographic tracings or by psychometric testing.

Data concerning the management and treatment of aldrin and dieldrin poisoning are available, and it would appear that the treatment of endrin poisoning is on similar lines. It is recommended that if aldrin or dieldrin has been ingested in any form the stomach should be washed out as quickly as possible, and that later adequate quantities of magnesium sulphate should be given in order that the ingested material may be purged rapidly. The patient should be closely watched for 72 hours, and at the first suggestion of involvement of the nervous system barbiturate therapy should be instituted. Barbiturates may be employed in the form of either sodium phenobarbitone or sodium amylobarbitone. Glucose may be administered intravenously, care being taken that not so much parenteral fluid is given as to encourage the production of pulmonary oedema. In cases either of acute or chronic intoxication a high-protein therapy may be advantageous, since liver damage may be produced by this type of poisoning. For this purpose the intravenous administration of amino-acids is recommended. The use of morphine is definitely contraindicated. Because this type of poisoning may in very severe cases result in the production of pulmonary oedema it may be necessary to institute oxygen therapy. In acute intoxications kidney damage may be manifested by the presence of haemolysed blood in the urine, therefore the benzidine test may be positive in the absence of red cells in the urine.

Although there is apparently no literature concerning human endrin poisoning, details of the mammalian toxicity of this substance have been published (Cole, 1955). It is stated that the acute oral toxicity of endrin to small laboratory animals is greater than that of aldrin or dieldrin, the LD_{50} to male rats being approximately 35 mg. per kg., and to female rats about half of this figure.

Summary

The investigation has established that a consignment of endrin dispatched on February 20, 1956, leaked 3 gallons (13.6 litres) into the conveying wagon in transit. The same wagon, which was used for the conveyance of empties between February 20 and April 25, was on the latter date loaded with sacks of flour at Cardiff and dispatched to Swansea. Of the 100 sacks carried in the wagon it was proved that two absorbed endrin from the vehicle floor, and both these sacks were delivered to one bakery as part of the weekly consignment. One of these sacks was returned, and endrin was found to be present in some parts of the flour to the extent of 5,500 parts per million. The other sack was used by the baker to manufacture loaves which caused 49 people to be ill enough to require medical treatment. Endrin was recovered from some parts of the bread consumed to the extent of 150 parts per million. It was further established that while in the bakery the empty contaminated sack which had contained national flour came into contact with dough made from patent white flour which, having been used to make white bread rolls, caused 10 men to become ill at a local works after consuming them.

Samples taken from the wagon floor and analysed on June 8 showed endrin still to be present in one section of the wagon to the extent of 116,000 parts per million.

The successful result of the inquiry would not have been achieved had the public health department not received the fullest assistance and co-operation from all the firms and organizations involved. It is desired to acknowledge the assistance provided by the Department of the Government Chemist, London, and the Glamorgan County Public Health Laboratory. The information on case histories was readily provided by Dr. Duncan Davies, medical superintendent, Morriston Hospital; Dr. Idwal Pugh, medical superintendent, Hill House Isolation Hospital, Swansea; and Mr. B. J. Baker, department of electroencephalography, Morriston Hospital.

REFERENCES

Cole, Leyland L. W. (1955). *World Crops*, 7, No. 4, p. 154.
Princi, F. (1952). "Human Toxicity of Certain Chlorinated Hydrocarbon Insecticides." Paper presented to 3rd International Congress of Phytopharmacy, Paris, September, 1952.
Spiotta, E. J. (1951). *A.M.A. Arch. industr. Hyg.*, 4, 560.

TREATMENT OF MEGALOBLASTIC ANAEMIA OF PREGNANCY AND THE PUERPERIUM WITH VITAMIN B_{12}

BY

E. B. ADAMS, M.B., B.Sc., M.R.C.P.
Professor of Medicine, University of Natal, Durban

Early reports from temperate climates indicated that treatment of megaloblastic anaemia of pregnancy and the puerperium with vitamin B_{12} was usually ineffective (Bethell *et al.*, 1948; Day *et al.*, 1949; Furman *et al.*, 1950; Ginsberg *et al.*, 1950; Ungley and Thompson, 1950; Clark, 1952). Total dosage did not exceed 120 μg. in the cases described. Later, however, a case was treated successfully in Holland with only 45 μg. (Nieweg, 1952), and recently in Dublin satisfactory responses followed the use of massive doses ranging from 900 to 5,000 μg. in 13 patients out of a series of 17 (Moore *et al.*, 1955). In warmer climates response to vitamin B_{12} in small amounts was often satisfactory (Patel and Kocher, 1950; Chaudhuri, 1951), and good results sometimes followed the use of larger doses (Cohen, 1953; Adams and Wilmot, 1953; Tasker, 1954; Berry 1955).

Kothari and Bhende (1949) believed that the disease commonly seen in India and the Tropics was the same as that described in Britain by Callender (1944). Diagnosis depended on the presence of megaloblasts of Ehrlich in the peripheral blood or bone marrow. Cases reported from most parts of the world usually responded well to treatment with folic acid, and there were clinical similarities. Differences in response to vitamin B_{12}, however, supported the views of Thompson and Ungley (1951) and others that there are several varieties of the condition, while the work of Foy *et al.* (1952a, 1952b) in East Africa showed differences in the appearance of the bone marrow.

This paper records the results of a clinical trial using large doses of vitamin B_{12} in 10 cases of the type of megaloblastic anaemia associated with pregnancy or the puerperium seen in Durban. The appearance of the bone marrow is briefly described.

Clinical Features

From a series of 34 patients with severe megaloblastic anaemia associated with pregnancy or the puerperium, 10 who were not dangerously ill were chosen for the trial. Two patients were African and eight Indian. Their ages and parity are indicated in Table I, which also shows the main findings in the blood on admission to hospital, and the results of gastric analysis after stimulation with histamine. Clinical features were similar to those previously described in our cases (Adams and Wilmot, 1953). These will not be discussed further except as regards infections and other factors which might be expected to retard recovery after treatment. Pyrexia was present in seven patients, all of whom were investigated for sources of infection. There was mild pyelitis in two (Cases 2 and 6); two others had complained of diarrhoea before admission, but no cause was found on stool examination. *X*-ray examination of the chest in nine patients revealed no abnormality. One patient had evidence of puerperal sepsis, which was not severe (Case 9), but pyrexia persisted after this had been cleared up. Full investigations revealed no cause, other than severe anaemia for this pyrexia, which settled when the blood count rose. In their series Badenoch *et al.* (1955) record a high incidence of other complications such as vomiting and haemorrhage, but these were absent from my cases. In the whole series of 34 cases there was no clinical evidence of steatorrhoea, an uncommon disease in South Africa; faecal fats estimated in 21 (six of the present trial series), were always within the normal range. It thus seems unlikely that infections or other factors have obscured the results of treatment in this trial.

TABLE I

Case No.	Age	Previous Pregnancies	Haemoglobin (g./100 ml.)	M.C.V. (Cubic μ)	M.C.H.C. (%)	Reticulocytes (%)	Serum Proteins (g./100 ml.)		Serum Bilirubin (mg./100 ml.)	Free Acid
							Total	Albumin		
1	29	5	3·9	89	25	0·5	8·1	4·8	0·8	++
2	26	1	3·2	98	36	1·2	7·0	4·0	0·4	++
3	20	0	3·1	96	36	1·6	7·3	3·4	0·6	++
4	28	10	5·6	106	27	4·4	7·9	3·4	0·2	++
5	35	5	3·2	125	32	3·3	6·0	2·6	0·9	+
6	26	0	4·4	144	35	5·4	6·6	3·5	0·8	+
7	43	7	6·9	93	33	2·3	6·0	3·2	0·8	+
8	33	8	4·4	97	35	1·3	5·8	2·5	2·9	+
9	20	0	6·5	111	34	1·4	4·7	2·3	0·7	+
10	30	9	4·4	135	33	5·9	5·6	2·5	0·4	+

Diet

Dietary histories are difficult to obtain and are not very reliable. Family incomes of all were low, and carbohydrate intake tended to be high. Protein was very low in seven, and apparently adequate in one (Case 6). One patient is of particular interest in view of the suggestion of Badenoch